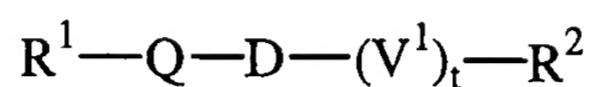


CLAIMS

What is claimed is:

5

1. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

10

R^1 and R^2 independently are selected from:

C_1 - C_6 alkyl;

Substituted C_1 - C_6 alkyl;

C_2 - C_6 alkenyl;

Substituted C_2 - C_6 alkenyl;

15

C_2 - C_6 alkynyl;

Substituted C_2 - C_6 alkynyl;

C_3 - C_6 cycloalkyl;

Substituted C_3 - C_6 cycloalkyl;

C_3 - C_6 cycloalkyl- $(C_1$ - C_6 alkylenyl);

20

Substituted C_3 - C_6 cycloalkyl- $(C_1$ - C_6 alkylenyl);

3- to 6-membered heterocycloalkyl;

Substituted 3- to 6-membered heterocycloalkyl;

3- to 6-membered heterocycloalkyl- $(C_1$ - C_6 alkylenyl);

Substituted 3- to 6-membered heterocycloalkyl- $(C_1$ - C_6 alkylenyl);

25

Phenyl- $(C_1$ - C_6 alkylenyl);

Substituted phenyl- $(C_1$ - C_6 alkylenyl);

Naphthyl- $(C_1$ - C_6 alkylenyl);

Substituted naphthyl- $(C_1$ - C_6 alkylenyl);

5-, 6-, 9-, and 10-membered heteroaryl- $(C_1$ - C_6 alkylenyl);

30

Substituted 5-, 6-, 9-, and 10-membered heteroaryl- $(C_1$ - C_6 alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

- Substituted naphthyl;
5-, 6-, 9-, and 10-membered heteroaryl;
Substituted 5-, 6-, 9-, and 10-membered heteroaryl;
 $R^3O-(C_1-C_6 \text{ alkylenyl})$;
5 Substituted $R^3O-(C_1-C_6 \text{ alkylenyl})$;
Phenyl- $O-(C_1-C_8 \text{ alkylenyl})$;
Substituted phenyl- $O-(C_1-C_8 \text{ alkylenyl})$;
Phenyl- $S-(C_1-C_8 \text{ alkylenyl})$;
Substituted phenyl- $S-(C_1-C_8 \text{ alkylenyl})$;
10 Phenyl- $S(O)-(C_1-C_8 \text{ alkylenyl})$;
Substituted phenyl- $S(O)-(C_1-C_8 \text{ alkylenyl})$;
Phenyl- $S(O)_2-(C_1-C_8 \text{ alkylenyl})$; and
Substituted phenyl- $S(O)_2-(C_1-C_8 \text{ alkylenyl})$;
wherein R^1 and R^2 are not both selected from:
15 C_1-C_6 alkyl;
 C_2-C_6 alkenyl;
 C_2-C_6 alkynyl; and
 C_3-C_6 cycloalkyl;
Each R^3 independently is selected from:
20 H;
 C_1-C_6 alkyl;
Substituted C_1-C_6 alkyl;
 C_3-C_6 cycloalkyl;
Substituted C_3-C_6 cycloalkyl;
25 Phenyl- $(C_1-C_6 \text{ alkylenyl})$;
Substituted phenyl- $(C_1-C_6 \text{ alkylenyl})$;
Naphthyl- $(C_1-C_6 \text{ alkylenyl})$;
Substituted naphthyl- $(C_1-C_6 \text{ alkylenyl})$;
5-, 6-, 9-, and 10-membered heteroaryl- $(C_1-C_6 \text{ alkylenyl})$;
30 Substituted 5-, 6-, 9-, and 10-membered heteroaryl- $(C_1-C_6 \text{ alkylenyl})$;
Phenyl;
Substituted phenyl;

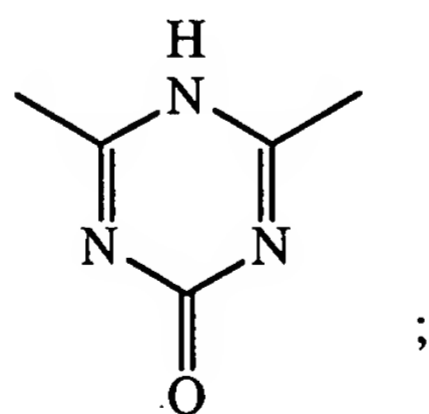
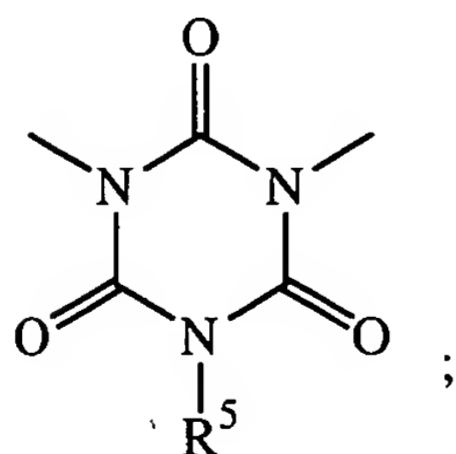
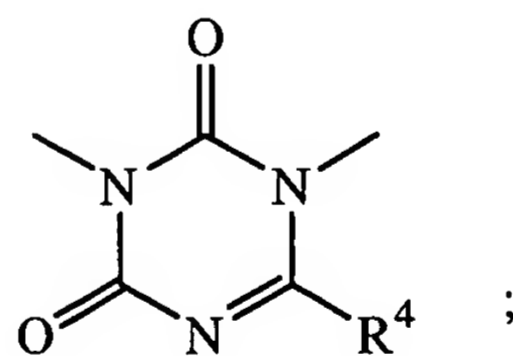
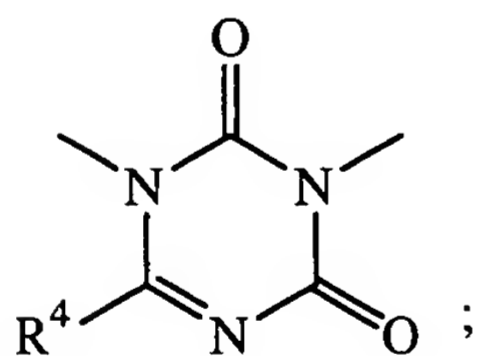
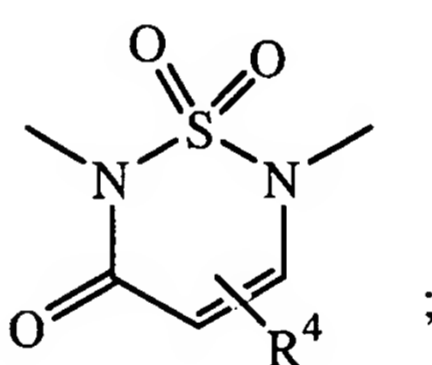
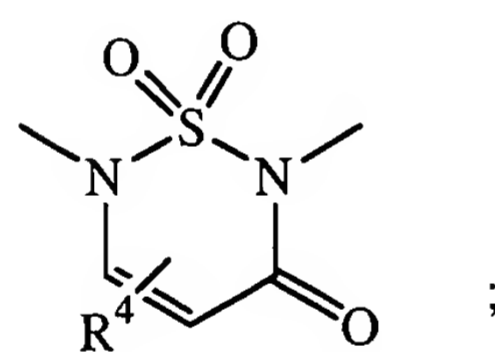
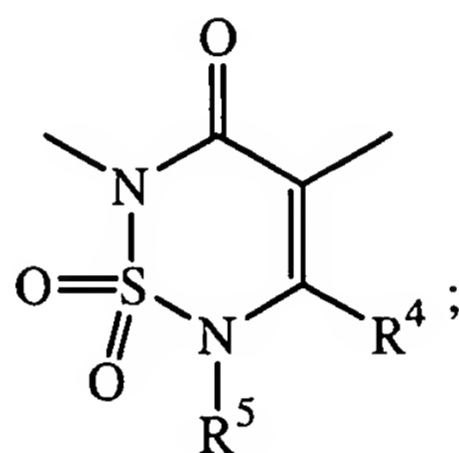
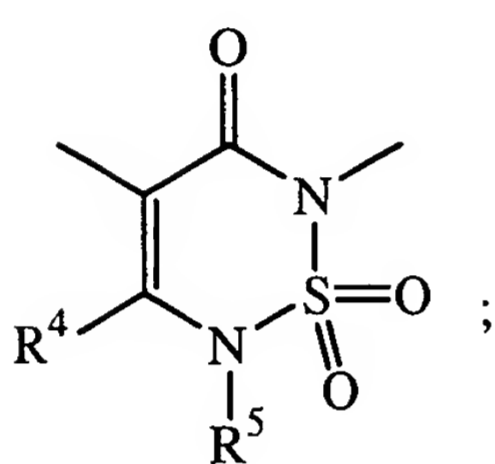
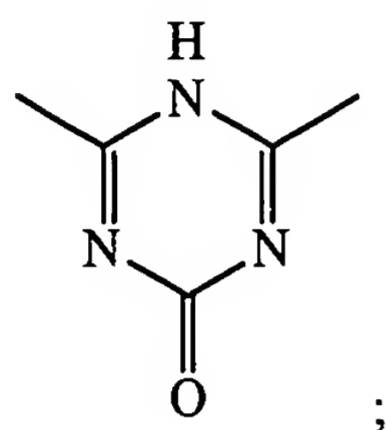
Naphthyl;

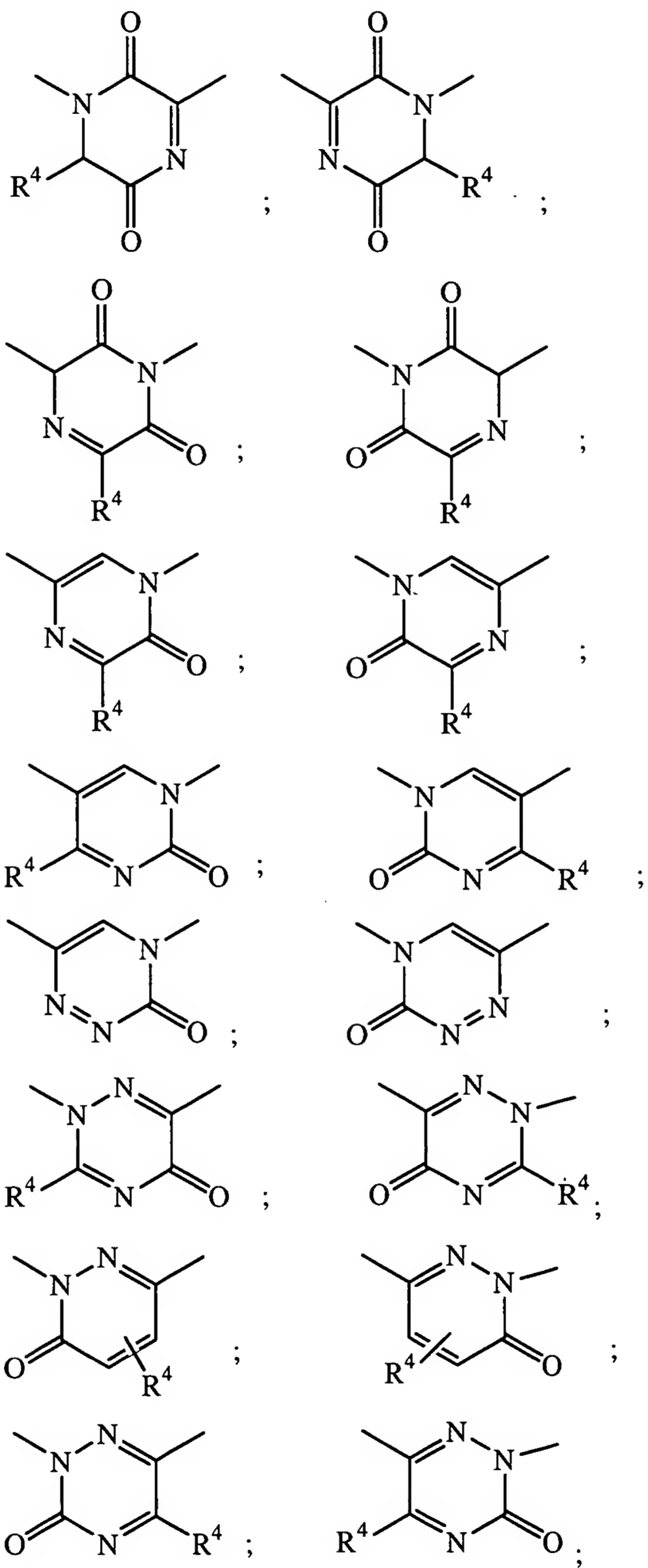
Substituted naphthyl;

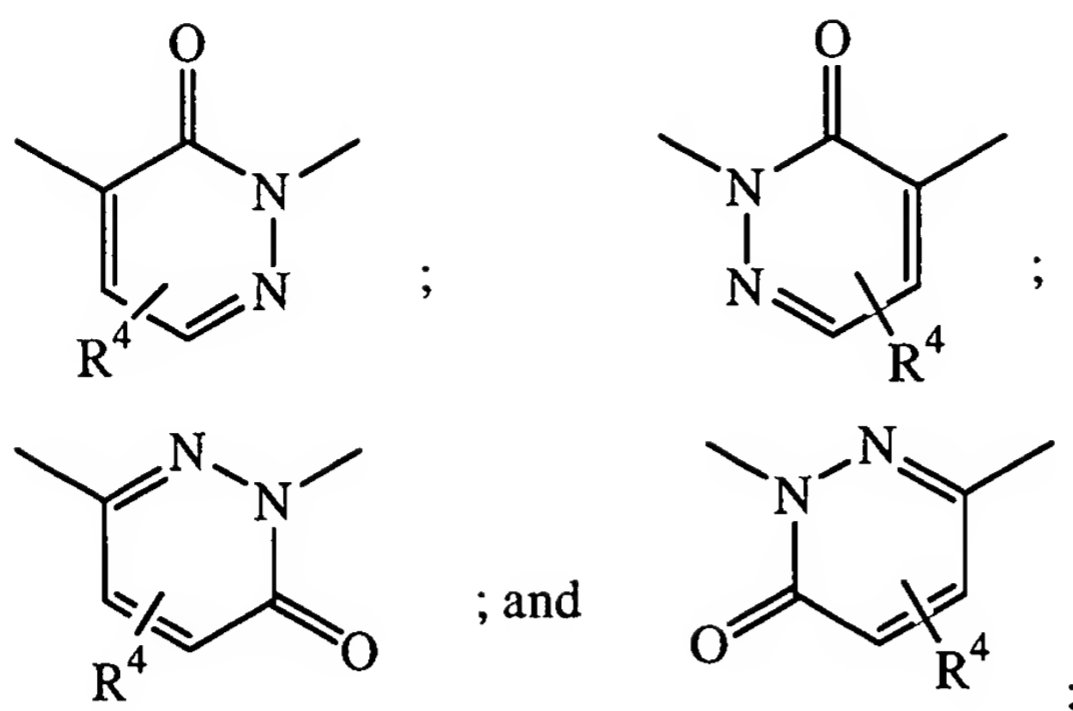
5-, 6-, 9-, and 10-membered heteroaryl;

Substituted 5-, 6-, 9-, and 10-membered heteroaryl;

5 D is a heteromonocyclic diradical:







Each R^4 independently is selected from:

- H;
- 5 F;
- CH₃;
- CF₃;
- C(O)H;
- CN;
- 10 HO;
- CH₃O;
- C(F)H₂O;
- C(H)F₂O; and
- CF₃O;

15 t is an integer of 0 or 1;

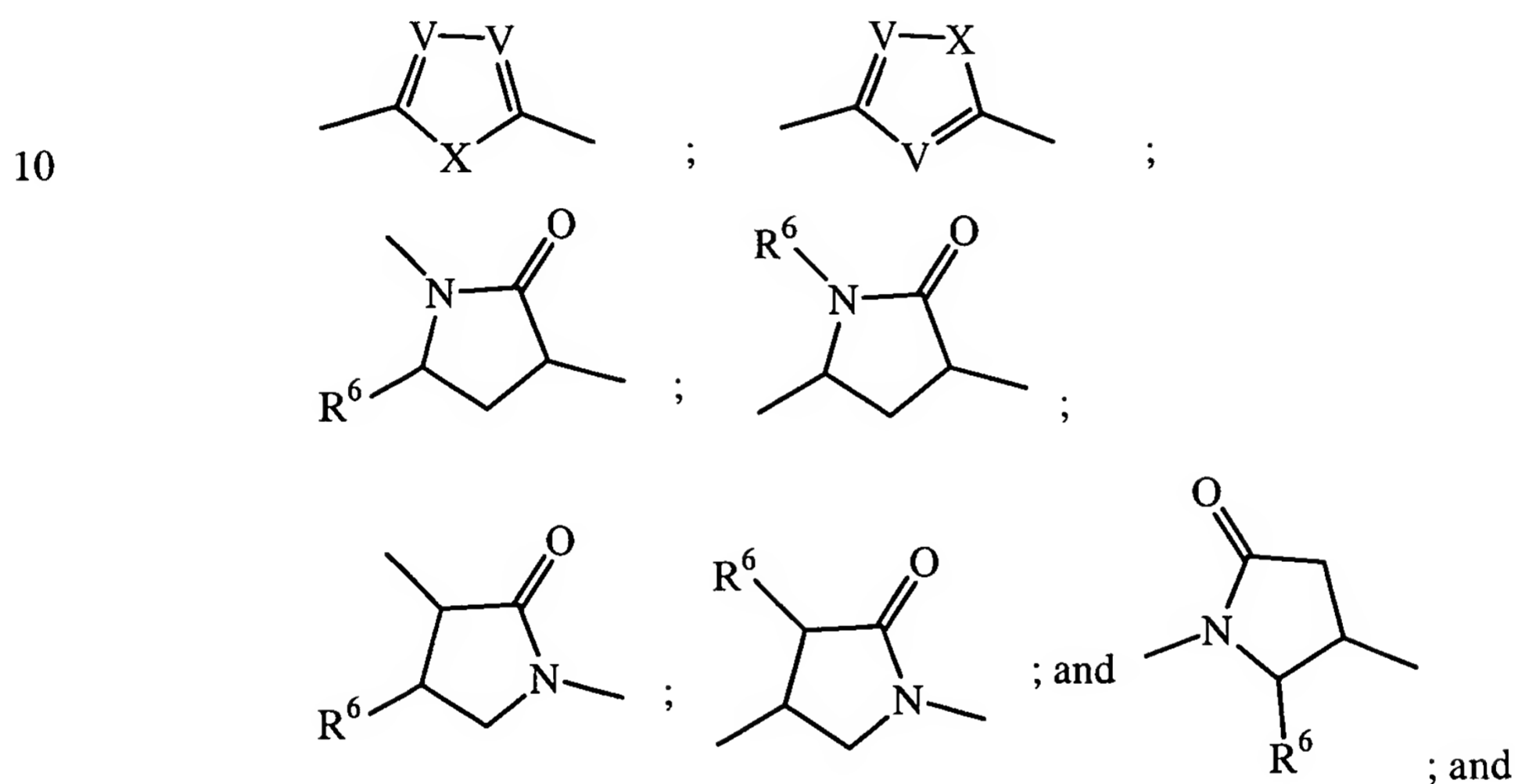
V^1 is selected from:

- a 5-membered heteroarylenyl;
- CH₂C≡C;
- CF₂C C≡C;
- 20 C(O)O;
- C(S)O;
- C(O)N(R⁵); and
- C(S)N(R⁵);

Q, when bonded to a nitrogen atom in group D, is selected from:

- 25 OC(O);
- CH(R⁶)C(O);
- OC(NR⁶);

5
 $\text{CH}(\text{R}^6)\text{C}(\text{NR}^6);$
 $\text{N}(\text{R}^6)\text{C}(\text{O});$
 $\text{N}(\text{R}^6)\text{C}(\text{S});$
 $\text{N}(\text{R}^6)\text{C}(\text{NR}^6);$
 $\text{SC}(\text{O});$
 $\text{CH}(\text{R}^6)\text{C}(\text{S});$
 $\text{SC}(\text{NR}^6);$
 $\text{C}\equiv\text{CCH}_2;$
 $\text{C}\equiv\text{CCF}_2;$



Q, when bonded to a carbon atom in group D, is as defined above and may further be selected from:

15
 $\text{OCH}_2;$
 $\text{N}(\text{R}^6)\text{CH}_2;$
 $\text{trans}-(\text{H})\text{C}=\text{C}(\text{H});$
 $\text{cis}-(\text{H})\text{C}=\text{C}(\text{H});$
 $\text{C}\equiv\text{C};$
 $\text{CH}_2\text{C}\equiv\text{C};$ and
20 $\text{CF}_2\text{C}\equiv\text{C};$

Each X independently is O, S, N(H), or N(C₁-C₆ alkyl);

Each V independently is C(H) or N;

Each R⁵ independently is H or C₁-C₆ alkyl;

R⁶ is H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl; 3- to 6-membered heterocycloalkyl;

phenyl; benzyl; or 5- or 6-membered heteroaryl;

Each "substituted" group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

- | | |
|----|--|
| 5 | C ₁ -C ₆ alkyl; |
| | C ₂ -C ₆ alkenyl; |
| | C ₂ -C ₆ alkynyl; |
| | C ₃ -C ₆ cycloalkyl; |
| | C ₃ -C ₆ cycloalkylmethyl; |
| 10 | Phenyl; |
| | Phenylmethyl; |
| | 3- to 6-membered heterocycloalkyl; |
| | 3- to 6-membered heterocycloalkylmethyl; |
| | cyano; |
| 15 | CF ₃ ; |
| | (C ₁ -C ₆ alkyl)-OC(O); |
| | HOCH ₂ ; |
| | (C ₁ -C ₆ alkyl)-OCH ₂ ; |
| | H ₂ NCH ₂ ; |
| 20 | (C ₁ -C ₆ alkyl)-N(H)CH ₂ ; |
| | (C ₁ -C ₆ alkyl) ₂ -NCH ₂ ; |
| | N(H) ₂ C(O); |
| | (C ₁ -C ₆ alkyl)-N(H)C(O); |
| | (C ₁ -C ₆ alkyl) ₂ -NC(O); |
| 25 | N(H) ₂ C(O)N(H); |
| | (C ₁ -C ₆ alkyl)-N(H)C(O)N(H); |
| | N(H) ₂ C(O)N(C ₁ -C ₆ alkyl); |
| | (C ₁ -C ₆ alkyl)-N(H)C(O)N(C ₁ -C ₆ alkyl); |
| | (C ₁ -C ₆ alkyl) ₂ -NC(O)N(H); |
| 30 | (C ₁ -C ₆ alkyl) ₂ -NC(O)N(C ₁ -C ₆ alkyl); |
| | N(H) ₂ C(O)O; |
| | (C ₁ -C ₆ alkyl)-N(H)C(O)O; |

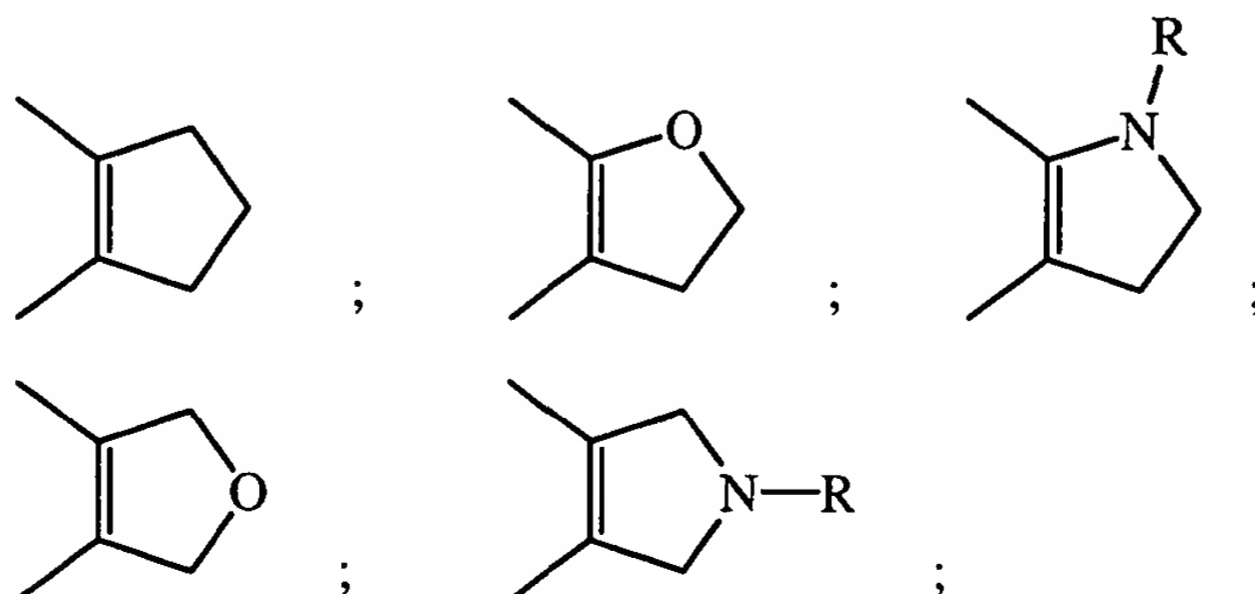
- (C₁-C₆ alkyl)₂-NC(O)O;
 HO;
 (C₁-C₆ alkyl)-O;
 CF₃O;
 5 CF₂(H)O;
 CF(H)₂O;
 H₂N;
 (C₁-C₆ alkyl)-N(H);
 (C₁-C₆ alkyl)₂-N;
 10 O₂N;
 (C₁-C₆ alkyl)-S;
 (C₁-C₆ alkyl)-S(O);
 (C₁-C₆ alkyl)-S(O)₂;
 (C₁-C₆ alkyl)₂-NS(O)₂;
 15 (C₁-C₆ alkyl)-S(O)₂-N(H)-C(O)-(C₁-C₈ alkylenyl)_m; and
 (C₁-C₆ alkyl)-C(O)-N(H)-S(O)₂-(C₁-C₈ alkylenyl)_m;

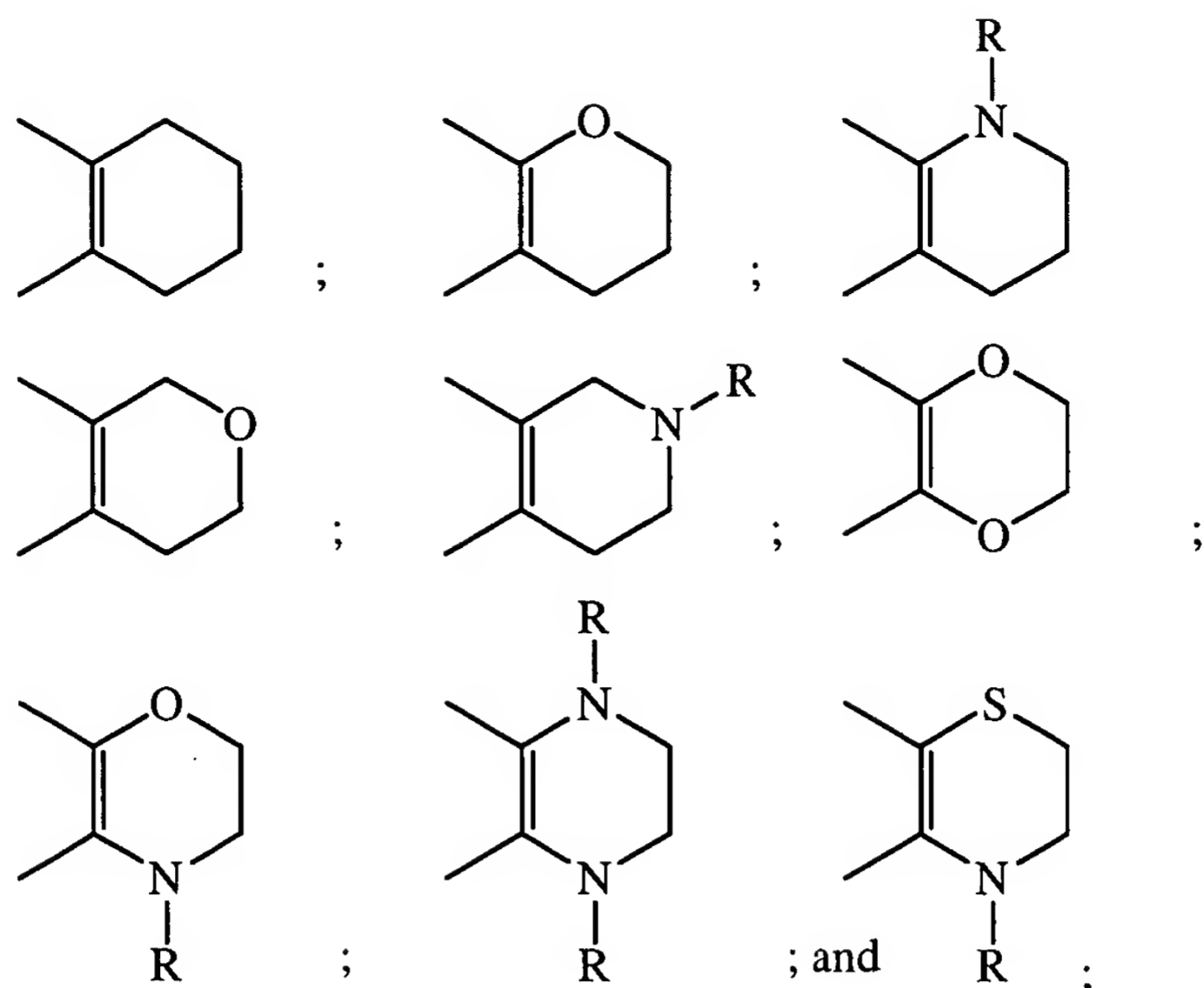
wherein each substituent on a carbon atom may further be independently selected from:

- Halo;
 20 HO₂C; and
 OCH₂O, wherein each O is bonded to adjacent carbon atoms to form a 5-membered ring;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

- 25 wherein two adjacent, substantially sp² carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:





Each m independently is an integer of 0 or 1;

5 R is H or C₁-C₆ alkyl;

wherein each 5-membered heteroarylenyl independently is a 5-membered ring containing carbon atoms and from 1 to 4 heteroatoms selected from 1 O, 1 S, 1 NH, 1 N(C₁-C₆ alkyl), and 4 N, wherein the O and S atoms are not both present, and wherein the heteroarylenyl may optionally be
 10 unsubstituted or substituted with 1 substituent selected from fluoro, methyl, hydroxy, trifluoromethyl, cyano, and acetyl;

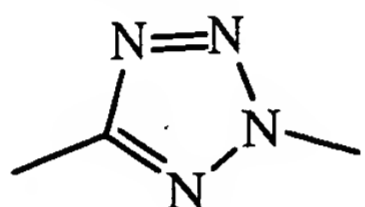
wherein each heterocycloalkyl is a ring that contains carbon atoms and 1 or 2 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 2 N(H), and 2 N(C₁-C₆ alkyl), and wherein when two O atoms or one O
 15 atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms
 20 and 1 or 2 heteroatoms independently selected from N, N(H), and N(C₁-C₆ alkyl), and 5- and 6-membered heteroaryl are monocyclic rings; and 9- and 10-membered heteroaryl are 6,5-fused and 6,6-fused bicyclic rings,

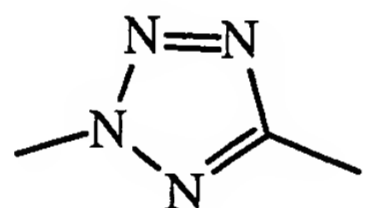
respectively, wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any (C₁-C₆ alkyl)₂-N group, the C₁-C₆ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and wherein each group and each substituent recited above is independently selected.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein V¹ is



3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein V¹ is



4. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is N(R⁶)C(O).

5. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is C≡C.

6. The compound according to any one of Claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein at least one of R¹ and R² is independently selected from:

Phenyl-(C₁-C₆ alkylenyl); and

Substituted phenyl-(C₁-C₆ alkylenyl);

wherein each group and each substituent is independently selected.

7. The compound according to any one of Claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein at least one of R^1 and R^2 is independently selected from:

5-, 6-, 9-, and 10-membered heteroaryl-(C_1 - C_6 alkylenyl); and

5 Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C_1 - C_6 alkylenyl);

wherein each heteroaryl contains carbon atoms and from 1 to 4 heteroatoms

independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1 - C_6 alkyl), and 4 N,

and 5- and 6-membered heteroaryl are monocyclic rings and 9- and 10-

membered heteroaryl are 6,5-fused and 6,6-fused bicyclic rings,

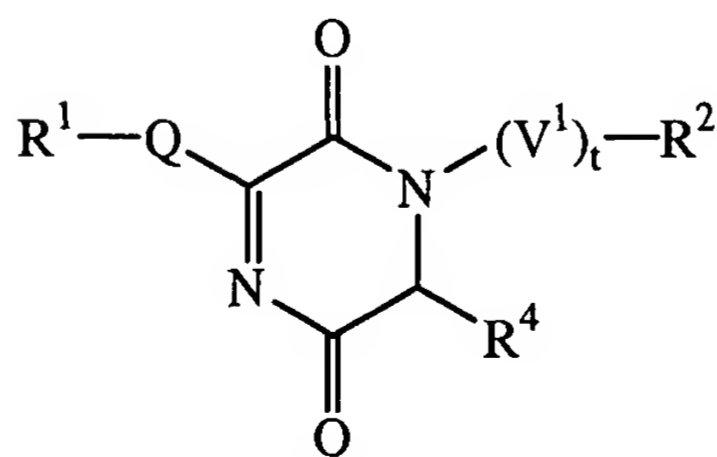
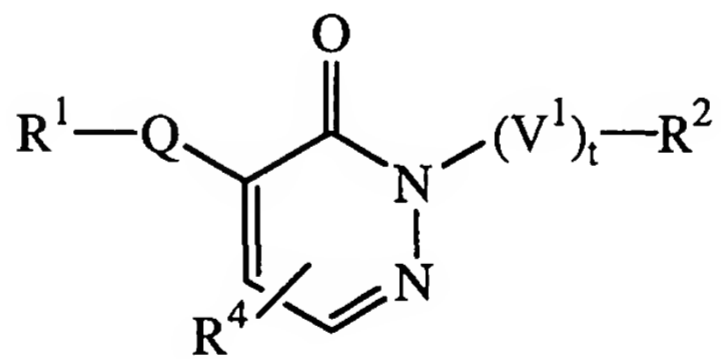
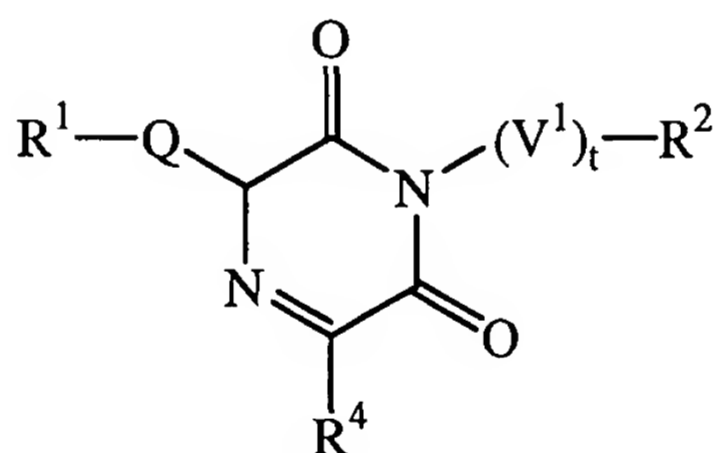
10 respectively, wherein at least 1 of the 2 fused rings of a bicyclic ring is

aromatic, and wherein when the O and S atoms both are present, the O and

S atoms are not bonded to each other; and

wherein each group and each substituent is independently selected.

15 8. A compound of Formula II, III, IV, V, or VI



$$\text{R}^1-\text{Q}-\text{N}-\text{N}=\text{C}(\text{V}^1)_t-\text{R}^2$$

VI

or a pharmaceutically acceptable salt thereof.

- 5 9. The compound of Formula II according to Claim 8, selected from:
4-[5-(3-Benzylcarbamoyl-2,6-dioxo-3,6-dihydro-2H-pyrazin-1-yl)-
tetrazol-2-yl]-benzoic acid;
4-(5-{2,6-Dioxo-3-[(pyridin-4-ylmethyl)-carbamoyl]-3,6-dihydro-2H-
pyrazin-1-yl}-tetrazol-2-yl)-benzoic acid;
10 4-[3-(3-Benzylcarbamoyl-2,6-dioxo-3,6-dihydro-2H-pyrazin-1-yl)-prop-2-
ynyl]-benzoic acid;
4-(3-{2,6-Dioxo-3-[(pyridin-4-ylmethyl)-carbamoyl]-3,6-dihydro-2H-
pyrazin-1-yl}-prop-2-ynyl)-benzoic acid;
4-{2-[2,6-Dioxo-3-(3-phenyl-prop-1-ynyl)-3,6-dihydro-2H-pyrazin-1-yl]-
15 oxazol-5-yl}-benzoic acid;
4-{2-[3-(3-Imidazol-1-yl-prop-1-ynyl)-2,6-dioxo-3,6-dihydro-2H-pyrazin-
1-yl]-oxazol-4-yl}-benzoic acid;
4-{3-[2,6-Dioxo-3-(3-phenyl-prop-1-ynyl)-3,6-dihydro-2H-pyrazin-1-yl]-
prop-2-ynyl}-benzoic acid;
20 4-{3-[3-(3-Imidazol-1-yl-prop-1-ynyl)-2,6-dioxo-3,6-dihydro-2H-pyrazin-
1-yl]-prop-2-ynyl}-benzoic acid;
4-({[2,6-Dioxo-3-(5-phenyl-oxazol-2-yl)-3,6-dihydro-2H-pyrazine-1-
carbonyl]-amino}-methyl)-benzoic acid;
4-{3-[2,6-Dioxo-3-(5-phenyl-oxazol-2-yl)-3,6-dihydro-2H-pyrazin-1-yl]-
25 prop-2-ynyl}-benzoic acid;
4-{5-[2,6-Dioxo-3-(4-phenyl-oxazol-2-yl)-3,6-dihydro-2H-pyrazin-1-yl]-
tetrazol-2-yl}-benzoic acid; and

4-{3-[2,6-Dioxo-3-(4-phenyl-oxazol-2-yl)-3,6-dihydro-2H-pyrazin-1-yl]-
prop-2-ynyl}-benzoic acid;

or a pharmaceutically acceptable salt thereof.

- 5 10. The compound of Formula III according to Claim 8, selected from:
- 4-[5-(5-Benzylcarbamoyl-6-oxo-6H-pyridazin-1-yl)-tetrazol-2-yl]-benzoic
acid;
- 4-(5-{6-Oxo-5-[(pyridin-4-ylmethyl)-carbamoyl]-6H-pyridazin-1-yl}-
tetrazol-2-yl)-benzoic acid;
- 10 4-[3-(5-Benzylcarbamoyl-6-oxo-6H-pyridazin-1-yl)-prop-2-ynyl]-benzoic
acid;
- 4-(3-{6-Oxo-5-[(pyridin-4-ylmethyl)-carbamoyl]-6H-pyridazin-1-yl}-
prop-2-ynyl)-benzoic acid;
- 15 4-{2-[6-Oxo-5-(3-phenyl-prop-1-ynyl)-6H-pyridazin-1-yl]-oxazol-5-yl}-
benzoic acid;
- 4-{2-[5-(3-Imidazol-1-yl-prop-1-ynyl)-6-oxo-6H-pyridazin-1-yl]-oxazol-
4-yl}-benzoic acid;
- 4-{3-[6-Oxo-5-(3-phenyl-prop-1-ynyl)-6H-pyridazin-1-yl]-prop-2-ynyl}-
benzoic acid;
- 20 4-{3-[5-(3-Imidazol-1-yl-prop-1-ynyl)-6-oxo-6H-pyridazin-1-yl]-prop-2-
ynyl}-benzoic acid;
- 4-({[6-Oxo-5-(5-phenyl-oxazol-2-yl)-6H-pyridazine-1-carbonyl]-amino}-
methyl)-benzoic acid;
- 4-{3-[6-Oxo-5-(5-phenyl-oxazol-2-yl)-6H-pyridazin-1-yl]-prop-2-ynyl}-
benzoic acid;
- 25 4-{5-[6-Oxo-5-(4-phenyl-oxazol-2-yl)-6H-pyridazin-1-yl]-tetrazol-2-yl}-
benzoic acid; and
- 4-{3-[6-Oxo-5-(4-phenyl-oxazol-2-yl)-6H-pyridazin-1-yl]-prop-2-ynyl}-
benzoic acid;
- 30 or a pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.
- 5 12. The pharmaceutical composition according to Claim 11, comprising a compound according to Claim 9 or 10, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.
- 10 13. A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.
- 15 14. The method according to Claim 13, wherein the compound administered is a compound according to Claim 9 or 10, or a pharmaceutically acceptable salt thereof.